124. A method according to claim 120, wherein the fragments are between 0.5 kb and 3.0 kb.

125. A method according to claim 120, wherein the fragments are sequenced by dideoxy sequencing.

126. A method according to claim 120, wherein the fragments are isolated by amplification using oligonucleotide primers.

REMARKS

Introduction

The following remarks are filed as a preliminary reply to issues raised in the prosecution of the parent application serial No. 08/971,344 and the grandparent application serial No. 08/216,538. The purpose of these remarks is to expedite prosecution by responding to issues raised in previous communications from the patent office. Applicants' have provided a new set of claims in an effort to more clearly define their invention.

The Invention

Applicants were the first to discover that because single nucleotide polymorphisms (SNPs) are densely and pervasively distributed throughout the genome of all species, SNPs could be used as genetic markers. The invention provides SNPs as genetic markers and methods of preparing genetic marker sets using SNPs. The invention further provides methods of constructing genetic maps, diagnosing disease, disease prognosis, trait association, identifying individuals, and determining parentage. These embodiments of the invention derive from the applicants' discovery of the distribution and density of SNPs in a mammalian genome and their penetrating insight that combining SNPs would provide valuable genetic information for any species. Before the invention, no-one understood or even contemplated that using a combination of SNPs could provide a powerful approach to genetic analysis. The

Applicants, in their specification, teach the advantageous properties of SNPs for genetic analysis. See the specification, for example, at pages 13-15. Moreover, the Applicants teach and demonstrate in their specification the additive power of using combinations of SNPs. See, for example, Figures 4 and 5. Applicants, in their specification, teach that even at high allelic frequencies, using combinations of SNPs provides highly accurate genetic analysis. See the specification, for example, at pages 38-42.

Added Claims

The added claims find support throughout the specification. Support for claims 54-70, SNPs as genetic markers, can be found throughout the specification. See for example page 41, lines 17-23 and page 43, lines 33-36. Support for claims 71–72, a method of genotyping, for example at page 4 of the specification. Claims 73-93, find support in the specification, for example, at pages 38-42. Support for claims 94-106, can be found, for example, in the specification at pages 42-45. Support for claims 107-112 can be found throughout the specification, for example at page 13, lines 23-32. Support for claims 113-126, directed to identifying SNPs in a genome of interest and determining allelic frequencies, can be found throughout the specification. See for example, the specification at pages 16-19. No new matter has been added.

Objection to the Specification

The Examiner has objected to the incorporation of essential material by reference to the abandoned U.S. Patent Application Serial No. 08/005,061. Applicants respectfully draw the Examiner's attention to section III (C), pp. 24-28 of this application, in which the relevant content of abandoned application 08/005,061 is included. In section III (C) the preferred method for preparation of single-stranded DNA primers is described. The specification has been amended for clarification, on page 34, lines 3-5, to specifically make note of the presence of the relevant material in section III(C) of this application. No new matter has been added by this amendment. Applicants respectfully submit that the Examiner's objection to the specification may properly be withdrawn.

Rejections Under 35 U.S.C. §112

In the Office Action of November 11, 1998, the Examiner rejected claims 34-39, 42-44, and 47-53 under 35 U.S.C. §112, first paragraph, for both written description and enablement.

Applicants have cancelled claims 34-39, 42-44, and 47-53 and provided a new set of claims. Applicants respectfully submit that the new set of claims more clearly define their invention. Applicants respectfully invite the Examiner to examine this new set of claims.

Applicants respectfully submit that the new claims are fully enabled by the specification and the specification provides written description for these claims. In the Office Action of November 11, 1998, the Examiner characterized the claims as analyzing SNPs and contended that the specification does not provide enablement for analyzing SNPs from other than equine DNA. The Applicants traverse such an argument since DNA does not chemically vary between species and the analysis of SNPs should not in any way depend on the source of the nucleic acid molecules. Moreover, the Applicants respectfully submit that the new claims, which are directed to SNPs as genetic markers and the use of SNPs in genetic analysis, find support throughout the specification and that the specification teaches the full scope of these claims to one skilled in the art. The Applicants' insight that combinations of SNPs would be extremely useful as genetic markers and for providing genetic analysis follows from their discovery regarding the distribution and density of SNPs in mammalian genomes. While the illustrative examples are directed to horse and human studies, one skilled in the art would readily understand that the methods and uses of SNPs, as provided by the invention, would be applicable to all species of plant and animal. The Applicants have described this general applicability throughout their specification. See for example, page 13, lines 23-33 and page 44, lines 29-36. Therefore, it is respectfully submitted that the new claims are fully taught and enabled by the Applicants' specification for all species of plant and animal.

Applicants' wish to make the Examiner aware of a clerical error in the specification, which is corrected by this amendment. The Examiner, in the Office Action, had stated that example 6 was directed to equine sequences. Example 6, in fact, provides an analysis of human SNPs. The section entitled "False Error Report" introduced into example 6 by a typographical error. One skilled in the art would recognize that the section entitled "False Error Report" found in example 6 is a duplication of the section found following example 5 and that it was introduced by a typographical error. The specification has been amended to remove this section which was mistakenly included with example 6.

Restriction Requirement

A restriction requirement was imposed in an Office Action mailed January 20, 1995, which was directed to the parent application 08/216,538. Applicants respectfully submit that the present claims are all directed to embodiments of the invention which relate to Applicants' recognition that combinations of SNPs can be used to provide powerful genetic analysis.

In view of the foregoing Amendment to the claims, and the remarks set forth above, reconsideration and allowance are respectfully solicited.

If the Examiner has any questions or suggestions of possible amendment for allowance, the Examiner is cordially invited to contact Applicants' attorney at the telephone number provided below.

Respectfully submitted,

Franklin S. Abrams
Registration No. 43,457
Attorney for Applicants

Tel: (212) 813-1600
Facsimile: (212) 813-9600